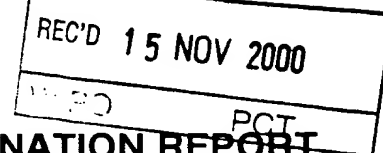


PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)



Applicant's or agent's file reference P.ULG.18/WO		FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/BE99/00105	International filing date (day/month/year) 12/08/1999	Priority date (day/month/year) 14/08/1998	
International Patent Classification (IPC) or national classification and IPC C12N15/76			
Applicant UNIVERSITE DE LIEGE et al.			

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 5 sheets, including this cover sheet.

- ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 2 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 04/02/2000	Date of completion of this report 13.11.00
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Wimmer, G Telephone No. +49 89 2399 7347 

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/BE99/00105

I. Basis of the report

1. This report has been drawn on the basis of *(substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).):*

Description, pages:

1-13 as originally filed

Claims, No.:

1-10 as received on 26/07/2000 with letter of 24/07/2000

Drawings, sheets:

1/3-3/3 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/BE99/00105

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-10
	No:	Claims	
Inventive step (IS)	Yes:	Claims	2-7
	No:	Claims	1
Industrial applicability (IA)	Yes:	Claims	2-10
	No:	Claims	

2. Citations and explanations
see separate sheet

Re Item V

Reasoned statement under Art. 35(2) PCT with regard to novelty, inventive step or industrial applicability.

The application does not meet the requirements of Art. 33 PCT since claims 1-10 do not appear to contain an inventive step.

- 1) Reference is made to the following documents (the document numbering corresponds to their order of citation in the international search report):

D1: VAN PEIJ N N M E ET AL: 'Isolation and analysis of xlnR, encoding a transcriptional activator co-ordinating xylanolytic expression in *Aspergillus niger*' MOLECULAR MICROBIOLOGY., vol. 27, no. 1, January 1998 (1998- 01), pages 131-142, XP000853720 OXFORD., GB

D2: GIANNOTTA F ET AL: 'A sequence-specific DNA-binding protein interacts with the xlnC upstream region of *Streptomyces* sp. strain EC3' FEMS MICROBIOLOGY LETTERS, vol. 142, 1996, pages 91-97, XP000853721 AMSTERDAM, NL ISSN: 0378-1097 cited in the application

Novelty under Art. 33(2) PCT.

- 2) The subject-matter of **claim 1** refers to a bacterial genetic sequence controlling in trans the expression of a bacterial xylanase-operator nucleotide sequence.

Although a transcriptional activator of xylanase genes had been cloned from eucaryotes (D1), this had not been done for an equivalent gene from bacteria.

Accordingly, claim 1, and consequently also claims 2-10, are considered to be novel.

Inventive Step under Art. 33(3) PCT.

- 3) Document D1 describes the isolation of the nucleic acid encoding a xylanase transactivator, xlnR, from *Aspergillus niger*. Consequently, the problem solved by the current application was the provision of a similar transactivator from an

alternative organism.

While document D2 proves the existence of a similar regulatory system in strains of *Streptomyces* (especially strain EC3), the document does not provide an isolated protein or partial coding sequence which would facilitate the isolation of the genetic sequence encoding the transactivator.

Therefore, the skilled person would be prompted to isolate a xylanase transactivator from *Streptomyces* strain EC3. The skilled person would do so through the application of standard techniques, such as cloning based on homology with the xlnR gene of D1, or through applying the method used by the authors of D1 to isolate xlnR from *Aspergillus*, in the isolation of the functionally similar gene from *Streptomyces*.

Since, however, the xlnR genes from *Aspergillus* and *Streptomyces* are unrelated, and since it appears dubious if application of the method of D1 would lead to success, it appears that considerable effort had been made in the isolation of the xlnR gene from *Streptomyces*.

Therefore, an inventive step is acknowledged for the provision of the *Streptomyces* xlnR coding sequence, and consequently, for claims 2-7.

- 4) However, while the sequence informations of the current application enable the skilled person to isolate homologous proteins and genes (as also covered by claims 2-7), the skilled person is not enabled to isolate bacterial xylanase transactivators *in general*. Therefore, and since the application does not include further examples of bacterial xlnR genes, the scope of claim 1 is found to be too broad, and the invention as described is non-enabling for claim 1.
Subject-matter of the claim is therefore found not to comply with art. 5 PCT.
- 5) As a consequence, an inventive step could therefore be acknowledged for claims 8-10 only if they refer to claims 2-4 or 2-7, respectively, but not to claim 1.

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CLAIMS

1. Isolated and purified bacterial genetic sequence (1) controlling in trans the expression of a xylanase promoter-operator bacterial nucleotide sequence (2).

2. Isolated and purified genetic sequence according to claim 1, being a nucleotide sequence which presents more than 60% homology with the nucleotide sequence SEQ ID NO 1 or its complementary strand.

3. Isolated and purified genetic sequence according to claim 2, which presents more than 80%, preferably more than 90%, more specifically more than 95%, homology with the nucleotide sequence SEQ ID NO 1 or its complementary strand.

4. Isolated and purified genetic sequence according to any one of the preceding claims, being the nucleotide sequence SEQ ID NO 1, its complementary strain or a portion thereof having more than 100 nucleotides and encoding a peptide controlling positively and/or negatively the activation of a xylanase promoter-operator nucleotide sequence.

5. Isolated and purified genetic sequence according to claim 1, being an amino-acid sequence which presents more than 60% homology with SEQ ID NO 2.

6. Isolated and purified genetic sequence according to claim 5, being an amino-acid sequence which presents more than 80%, preferably more than 90%, more specifically more than 95%, homology with SEQ ID NO 2.

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7. Isolated and purified genetic sequence according to claim 1, being the amino-acid sequence SEQ ID NO 2 or a portion thereof having more than 50 amino-acids which is capable of controlling positively and/or
5 negatively in trans the expression of a xylanase promoter-operator nucleotide sequence.

8. Nucleotide construct (6) comprising the isolated and purified nucleotide sequence according to any one of the claims 1 to 4, linked to a xylanase promoter-
10 operator nucleotide sequence (2) and possibly a nucleotide sequence (5) which is cis-activated by said xylanase promoter-operator nucleotide sequence (2).

9. Vector (7), preferably a plasmid, comprising the isolated and purified nucleotide sequence
15 (2) according to any one of the claims 1 to 7 or the nucleotide construct (6) according to claim 8.

10. Bacterial cell transformed by the vector according to claim 9 and which allows the expression of the isolated and purified genetic sequence according to any one
20 of the claims 1 to 7.